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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,807	07/29/2002	James Duncan Morrison	9013-46	2452
28120	7590	08/26/2004	EXAMINER	
ROPE & GRAY LLP			AUDET, MAURY A	
ONE INTERNATIONAL PLACE				
BOSTON, MA 02110-2624			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/088,807

Applicant(s)

MORRISON ET AL.

Examiner

Maury Audet

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2004 and 04/07/2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2 and 24-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2 and 24-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Response to Arguments and Amendment

Applicant's responses of June 08, 2004 and April 07, 2004 are acknowledged. Claims 2, and 24-42 remain pending. The invention is drawn to conjugation of peptides to the C-24 of bile acid/salt; wherein Applicant has elected insulin as the peptide species.

Claim Rejections - 35 USC § 103

Claims 2, and 24-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruff et al. (5,446,026) in view of Longenecker et al. (US 4,994,439) and Byun et al. (US 6,245,753).

Ruff et al. (as fully discussed in the PCT Search Report/Written Report of Applicant's PCT/GB00/02903) teach an amide of a bile salt wherein the group bound to the bile salt by the amide bond is a calcitonin decapeptide amide (see claims 1-7). Ruff et al. further discloses pharmaceutical compositions comprising this compound and their use for subcutaneous injection (see col. 2, lines 35-54, claims 8-11).

As discussed previously:

Longenecker et al. teach that “[i]t is by now well known that bile salts are capable of enhancing the absorption of peptides, such as insulin and other drugs, across the nasal mucous membrane and across the rectal and vaginal mucous membranes.

Byun et al. teach the conjugation of polysaccharides (such as heparin) to any bile acid at the free carboxyl group [C-24] and uses thereof, *for enhanced oral administration, and intestinal absorption.*

It would have been obvious to one of ordinary skill in the art at the time the invention was made to conjugate insulin at the C-24 carboxyl group for oral administration, of any bile acid in peptide-bile acid conjugates (conjugated at the free C-24 carboxyl group of bile acids) of Ruff et al., because Longenecker et al. teach the advantageous use of the peptide insulin with bile acids to enhance mucosal absorption of insulin. Furthermore, Byun et al. teach the advantageous use of other active agents conjugated to the C-24 of bile acid to enhance mucosal absorption of active agents (namely, polysaccharides (heparin) which Applicant had previously expressly included, among the myriad of peptides (or more aptly larger “pharmaceutical agents”, since enzymes and hormones are included therein also), as one of the key pharmaceutical agents which may benefit through absorption assistance by conjugation to bile acids).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant previously argued (in the response of April 7, 2004) that Longenecker et al. does not teach “conjugation” of insulin to bile acids, and that the reference should therefor be removed as a secondary reference. Since, Ruff et al. already teaches that peptides (*longer than 6 amino acids* in contradiction to Swaan et al.’s teachings as relied upon by Applicant) can be conjugated to the C-24 of bile acid, Longenecker et al. is merely provided as adequate support that the peptide of insulin would have been contemplated by one of skill in the art at the time of

the invention, as one of the peptides capable of being “conjugated” to the bile acid C-24 of Ruff et al.].

Additionally, Applicant’s arguments have been considered, but are not found persuasive. Applicant previously argued that Byun et al. is no longer applicable as a reference since Byun et al. only teach the conjugation of polysaccharides. Byun et al. is cited in the present action teaching that conjugation of active agents to bile acids at the C-24 can be administered orally to enhance mucosal administration.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Namely, Applicant’s deletion of “polysaccharides” as capable of being bound to the invention’s bile acid free carboxyl [C-24], removed Byun et al. as the best primary reference expressly teaching the “next found” species (polysaccharide, i.e. heparin) in Applicant’s general list of active agents capable of being conjugated to the C-24 of bile acid (since Applicant’s elected “insulin” was not found expressly, but rather intrinsically in Ruff et al. cited above). Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA

8/22/04



CHRISTOPHER R. TATE
PRIMARY EXAMINER